EXTENDED REPORT

Fibrin glue-assisted glaucoma drainage device surgery

M Y Kahook, R J Noecker

Br J Ophthalmol 2006;**90**:1486–1489. doi: 10.1136/bjo.2006.101253

See end of article for authors' affiliations

Correspondence to: M Y Kahook, Department of Ophthalmology, University of Colorado Health Sciences Center, Rocky Mountain Lions Eye Institute, 1675 N Ursula Lane, PO Box 6510, Mail Stop F-731, Aurora, CO 80045, USA; Malik.kahook@gmail.com

Accepted 4 August 2006
Published Online First 17 August 2006

Aim: To describe the use of fibrin glue as a suture substitute for portions of glaucoma drainage device (GDD) surgery.

Methods: Retrospective non-randomised case–control study reviewing 28 consecutive cases of GDD implantation using traditional suture material compared with 14 consecutive cases of GDD implantation using Tisseel fibrin glue (Baxter AG, Vienna, Austria) for portions of the procedure. The fibrin glue was used to close the conjunctiva, secure the pericardium patch graft and secure the tube to the sclera. Three-month follow-up data for each group as well as data on operating times, postoperative conjunctival inflammation, drugs used for glaucoma and intraocular pressure (IOP) were evaluated. Statistical analysis was carried out using analysis of variance.

Results: The mean (SD) age of the patients in the suture group (17 men and 11 women) was 56.6 (10.5) years and that in the Tisseel-assisted group (8 men and 6 women) was 54.7 (8.6) years ($p = 0.56$). No significant differences were observed in IOP levels at any time point between the two groups. No significant differences were found for the need for postoperative glaucoma drops or postoperative complication rates in both groups. Conjunctival inflammation was more pronounced in the suture group ($p = 0.002$) using a standard scale for comparison. The mean (SD) time of surgery was significantly less for the Tisseel-assisted group, 15.0 (3.11) min, than for the suture group, 25.93 (4.04) min ($p < 0.001$).

Conclusions: Tisseel fibrin glue seems to be a safe substitute for some of the sutures used in GDD surgery. Use of Tisseel seems to have no effect on IOP control or complications, whereas it considerably improved postoperative conjunctival inflammation and reduced time of surgery. Further studies are needed to better understand the role of fibrin glue in GDD implantation.

Glaucoma drainage device (GDD) implantation is a surgical treatment option for refractory glaucoma. It is common practice to use both absorbable and non-absorbable sutures throughout drainage device implantation procedures. Suture material is typically used for securing the plate to the sclera, securing the tube to the sclera, suturing a patch graft or scleral flap over the silicone tube and for conjunctival closure. Depending on the suture material used, the postoperative course can be marked by considerable discomfort caused by the conjunctival suture material. Additionally, absorbable suture material can induce inflammation, with localised surface and subconjunctival fibrosis creating an uneven conjunctival surface and excessive scarring.[1] Non-absorbable suture can erode through tissue postoperatively. Suturing the conjunctiva can compromise tissue that may be necessary for coverage or can cause complications such as buttonholes and tears. In addition, suturing the conjunctiva can sometimes be the most time-intensive portion of the surgery.

Fibrin glue has been used in ophthalmic surgery with success.[2–7] Although using fibrin glue as a substitute to suture may decrease GDD surgical time, there is concern about it not providing enough tensile strength to keep a patch graft or conjunctiva in place. Additionally, the use of fibrin glue may be cumbersome and require a great deal of coordination by operating room staff and doctors. We investigated the use of commercially available fibrin glue as a suture substitute for closure of the conjunctiva and placement of the patch graft during GDD implant surgery. Operating time, postoperative course, complication rate and clinical outcomes were compared between a group that had fibrin glue-assisted surgery and a group that received traditional suture material during GDD implantation.

METHODS

This was a retrospective non-randomised case–control study involving 14 consecutive patients who underwent GDD implantation with fibrin glue compared with 28 consecutive patients who received GDD implantation with traditional suture material between November 2005 and April 2006. Institutional review board exemption was obtained to review clinical data. The Baerveldt 250 mm^2 (Advanced Medical Optics, Santa Ana, California, USA) and Tutoplast (Innovative Ophthalmic Products, Costa Mesa, California, USA) were used in all patients.

The surgical procedure involved the creation of a limbal conjunctival peritomy of 100° in the superotemporal quadrant. After careful dissection posteriorly, the adjacent recti muscles were isolated with muscle hooks, and the Baerveldt wings were positioned underneath the muscles. In all cases, either 7-0 or 8-0 vicryl (polyglactin 910) suture was used to fasten the plate to the sclera, followed by cinching the silicone tube closed via external ligation. This was followed by placement of the tube into the anterior chamber through a sclerostomy created with a 23G needle. Tutoplast was sutured over the tube and the conjunctiva was re-approximated over the patch graft with the same vicryl suture used in previous steps.

The fibrin glue-assisted surgical technique was similar to that described for the vicryl suture group through the placement of the tube into the anterior chamber. At this point, Tisseel glue (Baxter AG, Vienna, Austria) was applied to the silicone tube to facilitate adherence to the underlying sclera. The glue was then applied to a 6×6 mm^2 of Tutoplast

Abbreviations: GDD, glaucoma drainage device; IOP, intraocular pressure

and over the tube entry site. The Tutoplast was placed over the tube and the glue was allowed to set. The conjunctiva was re-approximated to the limbus with non-toothed forceps. Tisseel was then applied to the underside of the conjunctiva and smooth forceps were used to hold the edges in place for 30 s until adherence was assured (fig 1A–C). A total of 1 cm^3 of Tisseel was used for each surgery. The eye was inspected for leaks as the anterior chamber was inflated to a proper pressure with balanced salt solution through a paracentesis. At the end of all surgeries in both groups, one drop each of prednisolone acetate 1%, atropine 1% and Zymar (gatifloxacin 0.3%) were instilled, followed by erythromycin ointment, an eye patch and shield.

Patients were followed-up at 1 day, 1 week, 1 month and 3 months postoperatively. Tube position, conjunctival surface inflammation, need for topical drugs for glaucoma, complications and intraocular pressure (IOP) were recorded for each patient. Conjunctival injection was measured on a scale of 0–4, with 0 representing no injection, 1 indicating mild hyperaemia, 2 indicating moderate hyperaemia, 3 indicating moderate to severe hyperaemia with tissue swelling and 4 representing extreme injection over the entire conjunctival flap, with engorgement of surface vessels. Operating room records and videotapes were also reviewed to determine total operative time in each patient. Summary statistics were calculated using data analysis software with Microsoft Excel. Analysis of variance and t tests were used to compare means between the two groups.

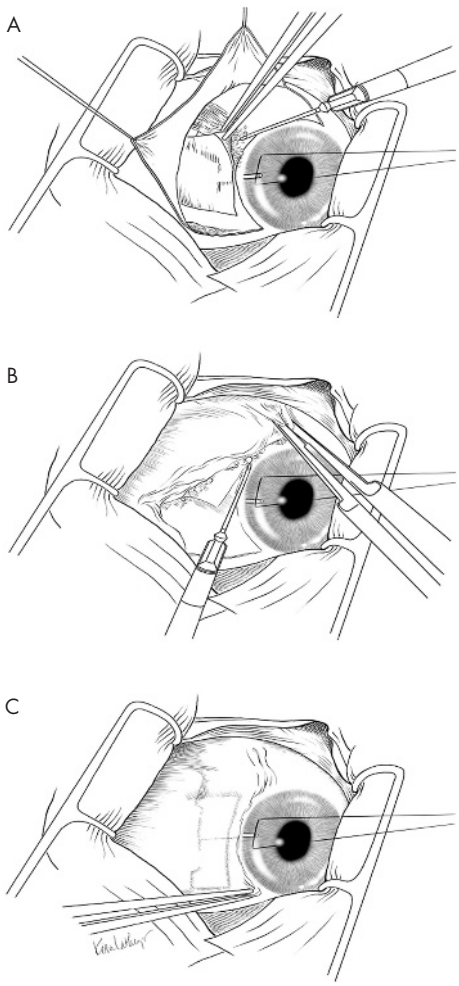

Figure 1 (A) The Tisseel glue is placed underneath the Tutoplast after securing the silicone tube to the sclera with the same glue material. (B) The Tisseel is then used to secure the conjunctiva to the sclera, (C) with the final result showing full approximation of the conjunctiva to the limbal edge.

RESULTS

Demographic characteristics were similar between the two groups. The suture group had 17 men and 11 women, whereas the Tisseel-assisted group had 8 men and 6 women. The mean (SD) age of the patients in the suture group was 56.6 (10.5) years and that in the Tisseel-assisted group was 54.7 (8.6) years ($p = 0.56$). Both groups included patients diagnosed with refractory glaucoma, including open angle (21 in the sutured group and 9 in the fibrin glue group), chronic angle closure (five in the suture group and three in the fibrin glue group), pseudoexfoliation (two in the suture group and one in the fibrin glue group) and traumatic glaucoma (one in the fibrin glue group). All but three patients had failed one previous trabeculectomy before undergoing GDD implantation. Three patients (two in the suture group and one in the fibrin glue group) who did not have previous trabeculectomy had previous penetrating keratoplasty; primary GDD implantation was chosen by the treating doctors for these patients. Visual acuity ranged between 20/20 and 20/400 for the suture group and 20/30 to light perception in the fibrin glue group. All surgeries were coperformed by the two authors using identical techniques.

No significant differences were observed in IOP between the groups at any time point from preoperative levels to 3 months of follow-up (table 1). The time of surgery was significantly less for the Tisseel group than for the suture group ($p<0.001$; table 2).

The conjunctiva of patients in the Tisseel group was consistently less injected and healed in a more even fashion (figs 2, 3). Conjunctival inflammation in the Tisseel group had a mean (SD) score of 2.0 (0.73) and that in the suture group was 2.83 (0.78). This difference between the two groups was significant ($p = 0.002$). Patients in the Tisseel group did not experience an increase in complication rates compared with the suture group. Specifically, there were no cases of plate, Tutoplast or tube displacement postoperatively, and the conjunctiva remained in place at all time points in both groups. No difference was found between groups in the number of postoperative hypotensive drops required (table 2). Visual acuity remained stable in all but three patients over the 3-month follow-up. One patient from the Tisseel group experienced a decrease in visual acuity from 20/60 to 20/100 owing to cataract progression. One patient from the suture group experienced a decrease in visual acuity from 20/80 to 20/200, caused by cataract progression. Finally, one patient from the suture group experienced improved vision from 20/80 to 20/50.

DISCUSSION

Tisseel glue is available in a kit containing freeze-dried powders and diluents. The two components making up this adhesive are a sealant protein component and a setting solution to activate the mixture. The sealant protein contains human fibrinogen, plasminogen, fibronectin and factor XIII in a bovine aprotinin solution. The setting solution is composed of human thrombin in calcium chloride solution. Once the thrombin solution comes in contact with the sealant protein component, fibrinogen is converted to fibrin and factor XIII cross links the fibrin. The fibrin and fibronectin cross link to collagen, thus leading to tissue–tissue adherence. Although other fibrin adhesives are available, such as BioGlue (CryoLife Europa, Hampshire, UK), Tisseel has been more extensively researched as a suture substitute in ophthalmic surgery than others.

Table 1 Analysis of intraocular pressure between the Tisseel and suture groups

Time	Tisseel group IOP	Suture group IOP	p Value
Preoperative	31.43 (7.01)	33.68 (7.54)	0.36
1 day PO	12.64 (4.29)	15.32 (7.01)	0.20
1 week PO	13.64 (3.82)	15.46 (4.87)	0.23
1 month PO	15.21 (2.94)	15.10 (3.44)	0.92
3 months PO	16.07 (3.52)	16.71 (2.46)	0.50

IOP, intraocular pressure; PO, postoperative.
Values are mean (SD).

Table 2 A comparison of surgical times, postoperative drops and inflammation between the two groups

	Tisseel group	Suture group	p Value
TOS (min)	15.00 (3.11)	25.93 (4.04)	<0.001
PO glaucoma drops	0.8 (1.5)	1.0 (1.2)	0.64
PO conjunctival inflammation	2.0 (0.73)	2.83 (0.78)	0.002

PO, postoperative; TOS, time of surgery.
Values are mean (SD).

In our technique, the Tisseel glue causes cross linking between the formed fibrin clot and the tissues on either side—namely, the conjunctiva and sclera. Although the tensile strength of Tisseel is not as great as vicryl or nylon sutures, the tissue is held in place for a sufficient period of time until collagen deposition and scarring occur.

Ophthalmic use of fibrin glue has been widely reported.[2 3] Lagoutte *et al*[2] used human fibrin glue for treatment of perforated and pre-perforated corneal ulcers. They viewed fibrin glue as a safe and effective alternative to immediate keratoplasty. Watts and Collin[3] reported on the use of human fibrin glue for full-thickness mucosal graft in inferior fornix reconstruction. The inherent properties of the glue allowed for a smooth surface postoperatively, as well as improved haemostasis.

Fibrin glue has also been specifically used in glaucoma surgery. Grewing and Mester[4] reported on the use of fibrin glue as a subconjunctival tamponade in cases of hypotony after trabeculectomy. Fibrin sealant was applied in the subconjunctival space over the scleral flap. The authors noted that both choroidal detachment and IOP improved with the eventual development of a functioning bleb. Asrani and Wilensky[5] reported on the treatment of bleb leaks with autologous fibrin tissue glue. Successful healing of bleb leaks was obtained in 9 of the 12 episodes in which fibrin tissue glue was used, and there were no statistically significant differences between fibrin glue and the other treatment modalities. They concluded that fibrin tissue glue offered a safe and efficacious treatment choice in caring for postoperative bleb leaks.

O'Sullivan *et al*[6] reported on the use of Tisseel glue for conjunctival wound closure after trabeculectomy. Tisseel was used in conjunction with sutures in four cases and alone in two cases, to achieve watertight closure of the conjunctiva. IOP was controlled in all cases, confirming that Tisseel was an effective method of achieving conjunctival wound closure after trabeculectomy.

A recent study by Valimaki[7] investigated the use of Tisseel fibrin glue as an adjunct in GDD implantation. The fibrin glue was used to prevent leaks around silicone tube entry sites when aqueous fluid was detected at the time of GDD implantation. This report concluded that intraoperative use of fibrin glue was a viable option for reducing peritubular filtration and for preventing immediate postoperative hypotony after drainage device implantation. Furthermore, they noted no difference in postoperative IOP control with Tisseel-assisted cases compared with their previous published data of

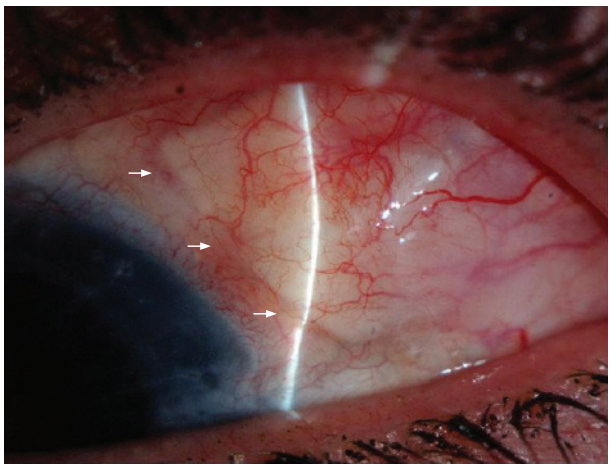

Figure 2 Baerveldt tube implantation with Tisseel glue 1 week postoperatively, showing mild injection of the conjunctiva, excellent approximation of the conjunctival edge to the limbus and proper positioning of the Tutoplast (arrows).

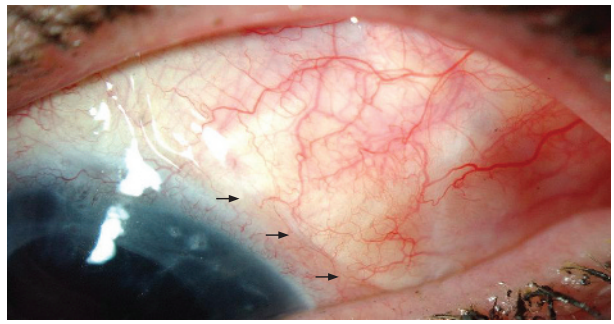

Figure 3 The patient from fig 2 showing a well-healed conjunctiva with Tutoplast (arrows) in place and very little surface inflammation 3 weeks later (1 month postoperatively).

drainage device implantation without Tisseel. The similar surgical outcomes with and without Tisseel suggested that adding fibrin glue to the surgical site did not increase postoperative fibroblast response to a level that affected IOP outcomes.

The tissue inflammatory response to the glue does not seem to be markedly worse than that observed with suture used for conjunctival closure. A study by Bahar *et al*[8] described the outcome of the use of a fibrin adhesive (Quixil, Omrix, Belgium) in penetrating trabeculectomy in a rabbit model and characterised the histological changes in fibrin glue versus nylon suture. The authors noted that the fibrin adhesive was easily identified histologically as an amorphic eosinophilic substance present up to 3 days post-operatively and nearly disappearing after 7 days. An acute inflammatory reaction was present up to 14 days, converting to chronic inflammation with collagen deposits after 30 days. The authors concluded that Quixil, not available in the US, caused no adverse effects on ocular tissue compared with nylon sutures.

The greatest benefits of using fibrin glue come at the time of surgery. The glue can be placed quickly and with minimal stretching or risk of buttonholing of the conjunctiva. It can be placed in areas in which it may be difficult to place a suture owing to the quantity or quality of the tissue or exposure. As a result, the total time of surgery can be reduced when Tisseel glue is used during the closure phase of the operation. On average, in our patients, operative time was decreased by over 10 min compared with cases using sutures exclusively. In our institution, the cost of operating room time is $46.26/min, resulting in a potential savings of over US$479/case. Each 1 cm^3 Tisseel kit costs approximately US$100, whereas sutures cost approximately US$10/pack. Overall, there is a potential average savings of over US$389 for each case.

Tisseel is not a panacea and there are several caveats regarding its use. The risk of transmitting infection through human components exists, although this, to our knowledge, has never been reported despite the use of Tisseel since 1974. Special equipment is necessary to heat the glue, and there is a learning curve for the staff to prepare it in a timely fashion. It can be difficult to localise its application, and there is a short window of time to position tissues correctly. Finally, the glue is expensive.

However, the potential efficiency that is gained and the patient comfort that is achieved is more than offset by the material cost of the glue. During the follow-up time in this study, the appearance and position of tissue early on—that is, during the first week—tended to predict the appearance up to 3 months. We did not note any cases of patch graft migration or conjunctival exposure in either group. After sutures dissolved or were removed, it was virtually impossible to tell which group had received glue and which had been sutured. Longer-term studies, in a prospective randomised fashion, are planned to tease out any differences that might exist between the two methods.

ACKNOWLEDGEMENTS

We thank Kira L Lathrop for her artistic contribution to fig 1.

Authors' affiliations

M Y Kahook, Department of Ophthalmology, University of Colorado Health Sciences Center, Rocky Mountain Lions Eye Institute, Colorado, USA

R J Noecker, UPMC Eye Center, Eye and Ear Institute, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA

Competing interests: None.

REFERENCES

1 **Biedner B**, Rosenthal G. Conjunctival closure in strabismus surgery: vicryl versus fibrin glue. *Ophthalmic Surg Lasers* 1996;**27**:967.
2 **Lagoutte FM**, Gauthier L, Comte PR. A fibrin sealant for perforated and preperforated corneal ulcers. *Br J Ophthalmol* 1989;**73**:757–61.
3 **Watts MT**, Collin R. The use of fibrin glue in mucous membrane grafting of the fornix. *Ophthalmic Surg* 1992;**23**:689–90.
4 **Grewing R**, Mester U. Fibrin sealant in the management of complicated hypotony after trabeculectomy. *Ophthalmic Surg Lasers* 1997;**28**:124–7.
5 **Asrani SG**, Wilensky JT. Management of bleb leaks after glaucoma filtering surgery. Use of autologous fibrin tissue glue as an alternative. *Ophthalmology* 1996;**103**:294–8.
6 **O'Sullivan F**, Dalton R, Rostron CK. Fibrin glue: an alternative method of wound closure in glaucoma surgery. *J Glaucoma* 1996;**5**:367–70.
7 **Valimaki J**. Fibrin glue for preventing immediate postoperative hypotony following glaucoma drainage implant surgery. *Acta Ophthalmol Scand* 2006;**84**:372–4.
8 **Bahar I**, Weinberger D, Lusky M, *et al*. Fibrin glue as a suture substitute: histological evaluation of trabeculectomy in rabbit eyes. *Curr Eye Res* 2006;**31**:31–6.